Chicken or the Egg: Anorexia Nervosa and Systemic Lupus Erythematosus in Children and Adolescents

**abstract**

Systemic lupus erythematosus (SLE) frequently has neuropsychiatric involvement including affective disorders, psychosis, and cognitive dysfunction. Evidence suggests that anorexia nervosa (AN) in adolescents with SLE may be triggered by steroid-induced changes in weight and body shape. We propose that AN may be another manifestation of neuropsychiatric SLE and should be considered in this patient population.

A retrospective chart review identified 7 children/adolescents diagnosed with SLE and the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition diagnostic criteria for AN, restrictive subtype, at the Hospital for Sick Children in Toronto between January 1989 and January 2011. One patient developed AN 15 months after being diagnosed with SLE that was attributed to prednisone-induced weight gain and cushingoid appearance. Of the remaining 6 patients, the median age at onset of AN symptoms was 12.2 years and diagnosis of AN was 13.6 years. The median age at SLE diagnosis was 14.2 years with median time after onset of AN symptoms of 20 months (7.5–32 months). All patients had evidence of joint symptoms and a positive antinuclear antibody, and 50% had lymphopenia at the time of SLE diagnosis. Treatment of SLE resulted in improvement of AN in all patients. The timing of the clinical presentation of AN in relation to SLE diagnosis and response to SLE treatment suggests that AN may be a novel presentation of neuropsychiatric SLE. Patients with AN who present with or develop joint symptoms, a positive antinuclear antibody, or lymphopenia should be investigated and followed for possible SLE.

PEDIATRICS 2014;133:e447–e450
Eating disorders (EDs) have been reported in association with several chronic medical conditions, including type 1 diabetes mellitus, celiac disease, chronic regional pain syndrome, and cystic fibrosis.1–4 Some controversy exists as to whether the association between EDs and chronic medical conditions is simply coincidental or whether certain medical conditions predispose to the development or expression of an ED. In adolescent girls with type 1 diabetes, the prevalence of EDs is nearly twice as high as their nondiabetic peers.5 A review of the histories of 326 adolescent girls with anorexia nervosa (AN) found a higher rate of preceding severe physical illness in adolescents with AN when compared with controls, suggesting that antecedent physical illness may be a risk factor for AN.6 Several mechanisms could explain how chronic illness may serve as a risk factor for the development of an ED. Developing a chronic illness in childhood or adolescence may negatively impact adolescents’ development psychologically, physiologically, and socially, thereby interrupting the normative adolescent developmental processes.6,7 The burden of a chronic illness combined with chronic dietary restraint, food preoccupation, interference with growth, pubertal delay, weight gain or loss during treatment, and impaired adolescent development could act as vulnerability factors and triggers for an ED.8 AN affecting children and adolescents with systemic lupus erythematosus (SLE) has been described in 2 case reports, but not at the time of the initial presentation of SLE.9,10 In both cases, AN did not present until after steroid-induced weight gain had occurred. In this series, we describe 7 patients with coexisting ED and SLE. Six of these patients developed signs and symptoms of AN before their SLE diagnosis, suggesting that AN may be a feature of SLE.

PATIENTS

The lupus clinic database at the Hospital for Sick Children in Toronto was searched for all patients with SLE who were diagnosed before age 18 with symptoms of AN before age 18 with symptoms of an ED followed between January 1989 and January 2011. A total of 7 female children/adolescents were diagnosed with SLE and AN over this 12-year period (total SLE cohort seen over this time was 425 patients; 78% were girls). Demographic data, clinical and laboratory manifestations of disease, including age at diagnosis, medications and treatments provided, and outcome, were recorded. Ethics approval was obtained from the Research Ethics Board at the Hospital for Sick Children (REB 1000023082).

All patients were followed by a single physician in the pediatric lupus clinic (EDS) and were assessed by using a standardized assessment protocol. Patients were diagnosed with an AN after clinical evaluation by a multidisciplinary team of child and adolescent ED experts spanning the fields of pediatrics, psychiatry, psychology, and dietetics. All patients met diagnostic criteria for AN as outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.

One patient was diagnosed with AN 15 months after being diagnosed with SLE and 12 months after starting prednisone. Her AN symptoms, including body image dissatisfaction, fear of fat, and desire to lose weight, were likely precipitated by steroid-induced weight gain, Cushinglike features, and teasing by classmates at school. The other 6 patients were diagnosed with AN either before or within 1 to 2 months of their SLE diagnosis. As a result, the patient who developed AN after treatment with prednisone was treated as an outlier and was not included in the data analysis, as the effect of prednisone on the development of an ED is not the focus of this article.

The key characteristics of the 6 patients are shown in Tables 1 and 2. The median age at onset of AN symptoms was 12.2 years (range 10–15.4 years). The

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**TABLE 1** Demographic Features of Cases

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<tr>
<th>Case</th>
<th>Age at Onset of AN Symptoms, y</th>
<th>Age at Diagnosis of AN, y</th>
<th>Age at Diagnosis of SLE, y</th>
<th>Time Elapsed Between AN Diagnosis and SLE Diagnosis, mo</th>
<th>BMI at Time of AN Diagnosis</th>
<th>Reason(s) for Rheumatology Referral</th>
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<tr>
<td>1</td>
<td>13.2</td>
<td>13.7</td>
<td>14.3</td>
<td>7.3</td>
<td>10.7</td>
<td>ESR 30, lymphopenia, anemia, ANA+</td>
</tr>
<tr>
<td>2</td>
<td>15.4</td>
<td>16.0</td>
<td>16.8</td>
<td>9.7</td>
<td>14.8</td>
<td>Persistent microscopic hematuria, ESR 15, ANA+</td>
</tr>
<tr>
<td>3</td>
<td>10.0</td>
<td>12.0</td>
<td>11.9</td>
<td>−1.0</td>
<td>16.0</td>
<td>SLE diagnosed first</td>
</tr>
<tr>
<td>4</td>
<td>11.4</td>
<td>14.0</td>
<td>14.1</td>
<td>0.7</td>
<td>15.6</td>
<td>Raynaud’s phenomenon, ANA+</td>
</tr>
<tr>
<td>5</td>
<td>13.0</td>
<td>13.5</td>
<td>15.4</td>
<td>22.9</td>
<td>14.8</td>
<td>CNS symptoms, malar rash, lymphopenia, ANA+</td>
</tr>
<tr>
<td>6</td>
<td>10.6</td>
<td>11.3</td>
<td>11.2</td>
<td>−1.5</td>
<td>13.0</td>
<td>SLE diagnosed first</td>
</tr>
<tr>
<td>Cohort mean (SD)</td>
<td>12.3 (2.0)</td>
<td>13.4 (1.6)</td>
<td>20.0 (9.0)</td>
<td>6.5 (9.2)</td>
<td>14.1 (2.0)</td>
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</table>

SLE clinical features: all patients had a positive ANA, arthritis, and lymphopenia, and/or Raynaud phenomenon at the time of diagnosis of SLE and had >4/11 American College of Rheumatology criteria for the classification of SLE (Table 2). In addition to AN, 5/6 patients had concurrent neuropsychiatric symptoms: None of the patients had signs or symptoms consistent with Sjögren syndrome, 2 had anti-Ro and 1 had anti-La antibodies. One patient had anti-cardiolipin antibodies, whereas the lupus anticoagulant was negative in all 6 patients. All patients had active disease as demonstrated by a Systemic Lupus Disease Activity Index score of ≥4. ESR, erythrocyte sedimentation rate.
The median age at AN diagnosis was 13.6 years (range 11.3 to 16 years). The median age at SLE diagnosis was 14.2 years (range 11.2 to 16.8 years). Onset of AN symptoms and diagnosis preceded SLE diagnosis by a median time of 19.7 months (range 7.4 to 32.0 months) and 4 months (range 1.5 to 22.9 months), respectively. All patients met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria for AN, restricting subtype. The median BMI at diagnosis of AN was 14.1 (range 10.7 to 16.0). All but 2 patients (cases 3 and 4) required admission to hospital for management of their AN. All patients were treated for their ED by an interdisciplinary team of child and adolescent ED experts as outpatients.

**DISCUSSION**

Neuropsychiatric disease may be the presenting symptom in children and adolescents with SLE with few other clinical features. Unlike what is seen in adults with SLE, mood and anxiety disorders are rarely seen in pediatric SLE. This article reports the first case series highlighting a novel association between AN and SLE. Symptoms of AN preceded the diagnosis of SLE by a median of 19.7 months, whereas AN diagnosis preceded the diagnosis of SLE by a median of 4 months.

There are only 2 previous case reports describing AN occurring in patients with SLE after steroid-induced weight gain, but before this publication not as an initial manifestation of SLE. This article reports the first case series highlighting a novel association between AN and SLE. Symptoms of AN preceded the diagnosis of SLE by a median of 19.7 months, whereas AN diagnosis preceded the diagnosis of SLE by a median of 4 months.

There is growing evidence implicating the immune system in the pathogenesis of EDs. One report showed that core psychobehavioral abnormalities characteristic of EDs correlated with the levels of autoantibodies against α-melanocyte-stimulating hormone, suggesting that AN may be associated with autoantibody-mediated dysfunction of primarily the melanocortin system. Other studies have shown...
that alterations of central and/or peripheral neuropeptidergic signaling are accompanied by disturbed regulation of body weight, appetite, or emotion.\textsuperscript{18,19} We suggest that AN in SLE can be a CNS manifestation of the disease and therefore this link between autoimmunity and EDs may have implications for future understanding of the pathogenesis and treatment of AN.

**CONCLUSIONS**

Our study demonstrates that in children and adolescents with AN, ongoing vigilance and monitoring for the emergence of joint symptoms, lymphopenia, positive antinuclear antibody (ANA), or a malar rash are prudent and should prompt an investigation for SLE. As it is well recognized that CNS involvement, even in the absence of classic manifestation of SLE, may be the initial presentation of pSLE, it is important for clinicians to consider that symptoms of AN may be the initial symptoms of pSLE as opposed to primary AN. Conversely, it is important to differentiate the anorexia and weight loss commonly seen in SLE from AN. Further research is needed to confirm that AN is a CNS manifestation of SLE.

**ACKNOWLEDGMENT**

Dr Silverman is the holder of the Ho Family Chair in Pediatric Autoimmune Diseases.

**REFERENCES**

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*Pediatrics* 2014;133;e447; originally published online January 6, 2014;
DOI: 10.1542/peds.2012-3048

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